Trying 3106016892...Open

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Dec 17	The CA Lexicon available in the CAPLUS and CA files
NEWS 3	Feb 06	Engineering Information Encompass files have new names
NEWS 4	Feb 16	TOXLINE no longer being updated
NEWS 5	Apr 23	Search Derwent WPINDEX by chemical structure
NEWS 6	Apr 23	PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
NEWS 7	May 07	DGENE Reload

NEWS EXPRESS	April 18 CURRENT WINDOWS VERSION IS V6.0, CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP), AND CURRENT DISCOVER FILE IS DATED 04/06
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:13:54 ON 17 MAY 2001

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'REGISTRY' ENTERED AT 14:14:00 ON 17 MAY 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 16 MAY 2001 HIGHEST RN 336099-02-6
DICTIONARY FILE UPDATES: 16 MAY 2001 HIGHEST RN 336099-02-6

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

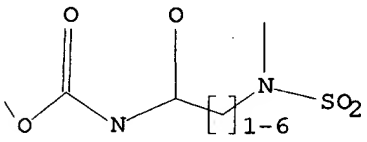
Structure search limits have been increased. See HELP SLIMIT for details.

=>
Uploading 591464b.str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam

SAMPLE SEARCH INITIATED 14:14:29 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 14:14:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 19 TO ITERATE

100.0% PROCESSED 19 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	133.56	133.71

STN INTERNATIONAL LOGOFF AT 14:14:47 ON 17 MAY 2001

09591464

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

```
=> s aspartyl protease
          4023 ASPARTYL
         68986 PROTEASE
L1         394 ASPARTYL PROTEASE
                (ASPARTYL(W)PROTEASE)

=> s l1 and aids
         40936 AIDS
L2          37 L1 AND AIDS

=> d 10-20 ibib abs hitstr
```

L2 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:808683 CAPLUS
DOCUMENT NUMBER: 132:49885
TITLE: Preparation of pyrones as protease inhibitors and antiviral agents
INVENTOR(S): Domagala, John Michael; Lunney, Elizabeth; Para, Kimberly Suzanne; Prasad, Josyula Venkata Nagendra Vara; Tait, Bradley Dean
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 155,028, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

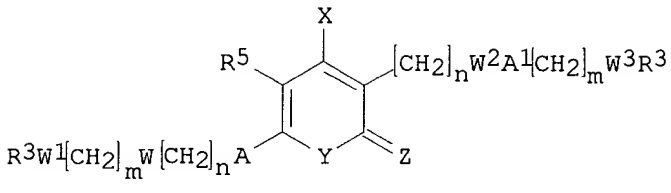
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6005103	A	19991221	US 1994-319769	19941012
CA 2176044	AA	19950526	CA 1994-2176044	19941026
WO 9514013	A1	19950526	WO 1994-US12257	19941026
W: AM, AU, BG, BY, CA, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, NO, NZ, PL, RO, RU, SI, SK, TJ, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9480911	A1	19950606	AU 1994-80911	19941026
AU 687465	B2	19980226		
EP 729465	A1	19960904	EP 1994-932042	19941026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09505293	T2	19970527	JP 1994-514457	19941026
HU 77719	A2	19980728	HU 1996-1350	19941026
ZA 9409147	A	19950721	ZA 1994-9147	19941117
ZA 9409150	A	19950731	ZA 1994-9150	19941117
FI 9602020	A	19960531	FI 1996-2020	19960513
NO 9602016	A	19960515	NO 1996-2016	19960515

09591464

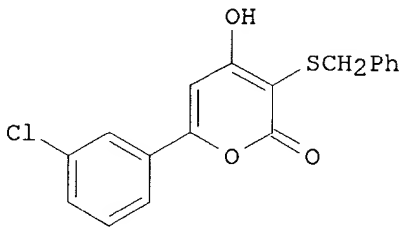
PRIORITY APPLN. INFO.: US 1993-155028 B2 19931119
US 1994-319769 A 19941012
WO 1994-US12257 W 19941026

OTHER SOURCE(S): MARPAT 132:49885

GI



I



II

AB The title compds. [I; X = OR1, NHR1, SR4, etc. (wherein R1 = R4, COR4; R4 = H, alkyl, cycloalkyl, etc.) Y = O, S; Z = O, S; A, A1 = a bond, (un)substituted Ph, naphthyl, etc.; R5 = H, alkyl, cycloalkyl, etc.; R3 = H, (CH2)pR4, (CH2)pA (p = 0-2); W, W1, W3 = a bond, O, CO, etc.; W2 = a bond, O, C.tplbond.C, etc.; m, n = 0-4] which potently inhibit the HIV **aspartyl protease** blocking HIV infectivity and therefore are useful in the development of therapies for the treatment of bacterial and viral infections and diseases, including **AIDS**, were prepd. E.g., synthesis of II which showed 50% HIV protease inhibition at 0.47 .mu.M, was given.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:705001 CAPLUS
DOCUMENT NUMBER: 131:322530
TITLE: Substituted tetronic acids useful for treating HIV and other retroviruses
INVENTOR(S): Chrusciel, Robert A.; Maggiora, Linda L.; Thaisrivongs, Suvit; Tustin, James M.; Smith, Clark W.; Tommasi, Ruben A.; Aristoff, Paul A.; Skulnick, Harvey I.; Howe, W. Jeffrey; Bundy, Gordon L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 116 pp., Cont.-in-part of U.S. Ser. No. 238,820, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

09591464

Connecting via Winsock to STN

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 25	Searching with the P indicator for Preparations
NEWS 4	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 5	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 6	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 7	Mar 08	Gene Names now available in BIOSIS
NEWS 8	Mar 22	TOXLIT no longer available
NEWS 9	Mar 22	TRCTHERMO no longer available
NEWS 10	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 11	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:55:36 ON 02 APR 2002

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:55:43 ON 02 APR 2002

09591464

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STRUCTURE FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6
DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.38	0.59

FILE 'CAPLUS' ENTERED AT 09:55:54 ON 02 APR 2002
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FILE COVERS 1907 - 2 Apr 2002 VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002 (20020330/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

09591464

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

```
=> s aspartyl protease
         4023 ASPARTYL
        68986 PROTEASE
L1        394 ASPARTYL PROTEASE
              (ASPARTYL(W)PROTEASE)

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        40936 AIDS
L2         37 L1 AND AIDS

=> d 10-20 ibib abs hitstr
```

L2 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:808683 CAPLUS
DOCUMENT NUMBER: 132:49885
TITLE: Preparation of pyrones as protease inhibitors and antiviral agents
INVENTOR(S): Domagala, John Michael; Lunney, Elizabeth; Para, Kimberly Suzanne; Prasad, Josyula Venkata Nagendra Vara; Tait, Bradley Dean
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 45 pp., Cont.-in-part of U.S. Ser. No. 155,028, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

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CA 2176044	AA	19950526	CA 1994-2176044	19941026
WO 9514013	A1	19950526	WO 1994-US12257	19941026
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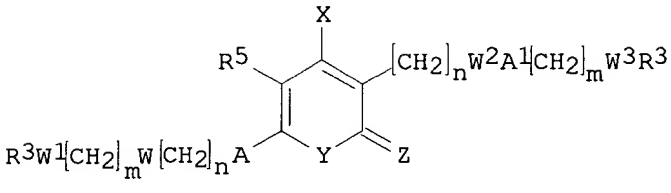
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9480911	A1	19950606	AU 1994-80911	19941026
AU 687465	B2	19980226		
EP 729465	A1	19960904	EP 1994-932042	19941026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09505293	T2	19970527	JP 1994-514457	19941026
HU 77719	A2	19980728	HU 1996-1350	19941026
ZA 9409147	A	19950721	ZA 1994-9147	19941117
ZA 9409150	A	19950731	ZA 1994-9150	19941117
FI 9602020	A	19960531	FI 1996-2020	19960513
NO 9602016	A	19960515	NO 1996-2016	19960515

PRIORITY APPLN. INFO.: US 1993-155028 B2 19931119
US 1994-319769 A 19941012
WO 1994-US12257 W 19941026
OTHER SOURCE(S): MARPAT 132:49885
GI



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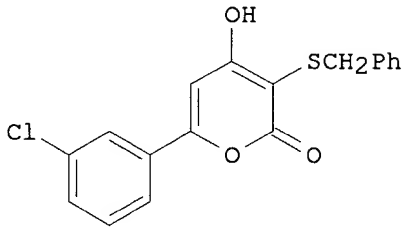


II

AB The title compds. [I; X = OR1, NHR1, SR4, etc. (wherein R1 = R4, COR4; R4 = H, alkyl, cycloalkyl, etc.) Y = O, S; Z = O, S; A, A1 = a bond, (un)substituted Ph, naphthyl, etc.; R5 = H, alkyl, cycloalkyl, etc.; R3 = H, (CH2)pR4, (CH2)pA (p = 0-2); W, W1, W3 = a bond, O, CO, etc.; W2 = a bond, O, C.tplbond.C, etc.; m, n = 0-4] which potently inhibit the HIV **aspartyl protease** blocking HIV infectivity and therefore are useful in the development of therapies for the treatment of bacterial and viral infections and diseases, including **AIDS**, were prepd. E.g., synthesis of II which showed 50% HIV protease inhibition at 0.47 .mu.M, was given.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:705001 CAPLUS
DOCUMENT NUMBER: 131:322530
TITLE: Substituted tetronic acids useful for treating HIV and other retroviruses
INVENTOR(S): Chrusciel, Robert A.; Maggiora, Linda L.; Thaisrivongs, Suvit; Tustin, James M.; Smith, Clark W.; Tommasi, Ruben A.; Aristoff, Paul A.; Skulnick, Harvey I.; Howe, W. Jeffrey; Bundy, Gordon L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 116 pp., Cont.-in-part of U.S. Ser. No. 238,820, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 5977169	A	19991102	US 1997-604937	19970728
ZA 9406099	A	19960212	ZA 1994-6099	19940812
WO 9507901	A1	19950323	WO 1994-US9533	19940907

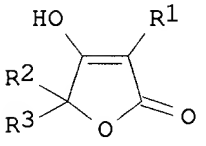
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN

RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1993-123029 19930917
US 1994-238820 19940506
WO 1994-US9533 19940907

OTHER SOURCE(S): MARPAT 131:322530

GI



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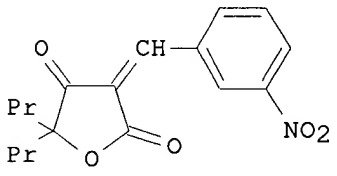
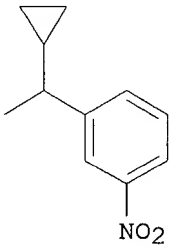
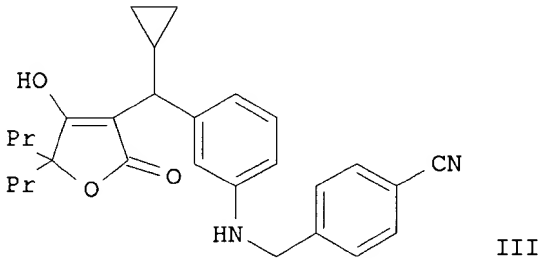


II

Q1=





III

AB The invention comprises novel substituted tetronic acid derivs. (I) and tautomers [wherein R1-R3 = wide variety of specified C-contg. substituents] that are inhibitors of HIV protease. I retard replication of any retrovirus contg. **aspartyl protease** and are useful for treatment of **AIDS** or **AIDS**-related diseases. Approx. 250 compds. are claimed, and phys. and biol. data for approx. 120 compds. are provided. For example, condensation of I [R1 = H, R2 = R3 = Pr] with 3-nitrobenzaldehyde gave >100% crude nitrobenzylidene deriv. II, which reacted with cyclopropylmagnesium bromide and CuBr.SMe2 in THF to give 62% I [R1 = Q1, R2 = R3 = Pr]. Hydrogenation of the nitro group (97%) and sulfonamidation of the resultant amino group with 4-cyanobenzenesulfonyl chloride (53%) gave title furandione III, a preferred compd. Several compds. including III are said to have inhibited replication of HIV-1IIIB in human cell lines. HIV-1 protease inhibitory data are provided, and over 100% inhibition was reported for many test compds. at doses as low as 3.3 .mu.M.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2002 ACS

09591464

ACCESSION NUMBER: 1999:692222 CAPLUS
DOCUMENT NUMBER: 132:30259
TITLE: Stereoselective hydroxylation of nonpeptidic HIV protease inhibitors by CYP2D6
AUTHOR(S): Zhao, Zhiyang; Koeplinger, Kenneth A.; Waldon, Daniel J.
CORPORATE SOURCE: Drug Metabolism Research, Pharmacia and Upjohn, Inc., Kalamazoo, MI, USA
SOURCE: Chirality (1999), 11(9), 731-739
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PNU-106893, N-{3-[1-(4-hydroxy-2-oxo-6-phenyl-6-propyl-5,6-dihydro-2H-pyran-3-yl)-2,2-dimethylpropyl]phenyl}-1-methyl-1H-imidazole-4-sulfonamide, is a selective HIV **aspartyl protease** inhibitor under evaluation as a potential oral treatment of acquired immunodeficiency disease. PNU-106893 is a mixt. of four stereoisomers, designated PNU-109165 (3.alpha.R, 6S), PNU-109166 (3.alpha.R, 6R), PNU-109167 (3.alpha.S, 6S), and PNU-109168 (3.alpha.S, 6R). The major P 450 isoforms involved in the metab. of PNU-106893 and its pure stereoisomers are identified as CYP2D6 and CYP3A4. The major oxidative biotransformation pathway of PNU-106893 which occurs in microsomal incubations appears to be hydroxylation of the phenylethyl side chain attached to the C-6 carbon of the dihydropyrone ring. This hydroxylation is mediated by CYP2D6 only and the process is stereoselective for the 6R abs. stereochem. The configuration at position 3 appears to play a minor role in the CYP2D6 mediated hydroxylation. These insights have impacted drug candidate selection for this class of compds.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:528340 CAPLUS
DOCUMENT NUMBER: 132:44526
TITLE: In vitro and in vivo anticandidal activity of human immunodeficiency virus protease inhibitors
AUTHOR(S): Cassone, Antonio; De Bernardis, Flavia; Torosantucci, Antonella; Tacconelli, Evelina; Tumbarello, Mario; Cauda, Roberto
CORPORATE SOURCE: Department of Bacteriology and Medical Mycology, Istituto Superiore di Sanita, Rome, 00161, Italy
SOURCE: Journal of Infectious Diseases (1999), 180(2), 448-453
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Highly active antiretroviral therapy that includes human immunodeficiency virus (HIV) **aspartyl protease** inhibitors (PIs) causes a decline in the incidence of some opportunistic infections in **AIDS**, and this decline is currently attributed to the restoration of specific immunity. The effect of two PIs (indinavir and ritonavir) on the enzymic activity of a secretory **aspartyl protease** (Sap) of Candida albicans (a major agent of mucosal disease in HIV-infected subjects) and on growth and exptl. pathogenicity of this fungus was evaluated. Both PIs strongly (.gtoreq.90%) and concn.-dependently (0.1-10 .mu.M) inhibited Sap activity and prodn. They also reduced Candida growth in a nitrogen-limited, Sap-expression-dependent growth medium and exerted a therapeutic effect in an exptl. model of vaginal candidiasis, with an efficacy comparable to that of

fluconazole. Thus, besides the expected immunorestoration, patients receiving PI therapy may benefit from a direct anticandidal activity of these drugs.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:460395 CAPLUS
DOCUMENT NUMBER: 131:106817
TITLE: Prodrugs of **aspartyl protease** inhibitors for treatment of HIV infections
INVENTOR(S): Hale, Michael R.; Tung, Roger D.; Baker, Christopher T.; Spaltenstein, Andrew; Furfine, Eric Steven; Kaldor, Istvan; Kazmierski, Wieslaw Mieczyslaw
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933795	A1	19990708	WO 1998-US27510	19981224
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9920121	A1	19990719	AU 1999-20121	19981224
PRIORITY APPLN. INFO.:			US 1997-70309P P	19971224
			WO 1998-US27510 W	19981224

OTHER SOURCE(S): MARPAT 131:106817
AB Prodrugs of a class of sulfonamides which are HIV **aspartyl protease** inhibitors are described. The prodrugs are characterized by favorable aq. soly., high oral bioavailability and facile in vivo generation of the active ingredient. The prodrugs and pharmaceutical compns. of this invention are particularly well suited for decreasing the pill burden and increasing patient compliance in HIV infections. E.g., a pharmaceutical compn., in addn. to a prodrug, may comprise an antiviral agent, a HIV protease inhibitor other than a compd. of this invention, and an immunostimulant.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:460393 CAPLUS
DOCUMENT NUMBER: 131:87804
TITLE: Preparation of 1,3-diacylamino-2-acyloxypropanes as prodrugs of **aspartyl protease** inhibitors.
INVENTOR(S): Hale, Michael R.; Tung, Roger D.; Baker, Christopher T.; Spaltenstein, Andrew; Furfine, Eric Steven; Kaldor, Istvan; Kazmierski, Wieslaw Mieczyslaw
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

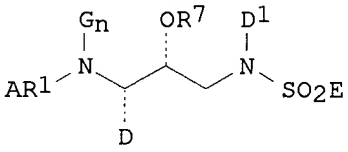
09591464

SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933793	A2	19990708	WO 1998-US27424	19981223
WO 9933793	A3	19990910		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2316218	AA	19990708	CA 1998-2316218	19981223
AU 9920925	A1	19990719	AU 1999-20925	19981223
BR 9814484	A	20001010	BR 1998-14484	19981223
EP 1042280	A2	20001011	EP 1998-965466	19981223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001527062	T2	20011225	JP 2000-526477	19981223
NO 2000003332	A	20000818	NO 2000-3332	20000626

PRIORITY APPLN. INFO.: US 1997-68889P P 19971224
WO 1998-US27424 W 19981223

OTHER SOURCE(S): MARPAT 131:87804
GI



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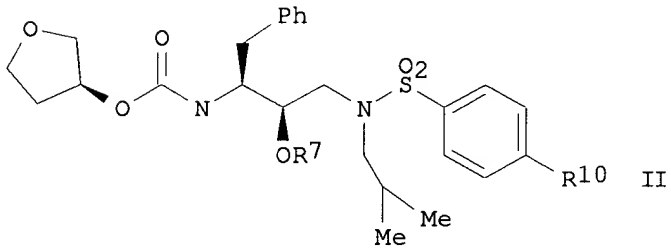


II

AB Title compds. [I; R1 = CO, SO2, COCO, O2C, OSO2, NR2SO2, etc.; A = (benzo- or heterocyclo-fused) 5-7 membered heterocyclyl(alkyl); D, D1 = Q, (substituted) alkyl, alkenyl, cycloalkyl, cycloalkenyl; G = H, R7, alkyl; E = Ht, OHt, HtHt, OR3, NR2R3, (substituted) alkyl, alkenyl, carbocyclyl, etc.; GR7 = atoms to form a heterocyclic ring; Q = (substituted) (unsatd.)

3-7 membered carbocyclyl, 5-7 membered heterocyclyl; R2 = H, (Q-substituted) alkyl; R3 = H, (substituted) Ht, alkyl, alkenyl; R7 = (CH2O)nY(ZM)(:X)ZMn, (CH2O)nCO(R9)nM1; M = H, Li, Na, K, Mg, Ca, Ba, ammonio, alkyl, alkenyl, etc.; M1 = H, (substituted) alkyl, alkenyl, etc.; R9 = C(R2)2, O, NR2; Y = P, S; X = O, S; Ht = cycloalkyl, cycloalkenyl, (substituted) aryl, 5-7 membered heterocyclyl; n = 0, 1; with provisos], were prepd. Thus, title compd. (II; R7 = H; R10 = NO2) was heated with H3PO3 and DCC in pyridine to give 96% II (R7 = OP(O)(OH)H; R10 = NO2). This was heated with TMSOOTMS and (TMS)2NH to give 88% II (R7 = OP(O)(OH)2; R10 = NO2). The latter was hydrogenated and salified to give II (R7 = OP(O)(ONa)2; R10 = NH2) (III). III in a methylcellulose/EtOH/H2O formulation administered orally to dogs showed a relative availability of 60.4% relative to its metabolite VS-478.

L2 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:460392 CAPLUS
DOCUMENT NUMBER: 131:87803
TITLE: Preparation of 1,3-diacylamino-2-acyloxypropanes as prodrugs of **aspartyl protease** inhibitors.
INVENTOR(S): Hale, Michael R.; Tung, Roger D.; Baker, Christopher T.; Spaltenstein, Andrew; Furfine, Eric Steven; Kaldor, Istvan; Kazmierski, Wieslaw Mieczyslaw
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

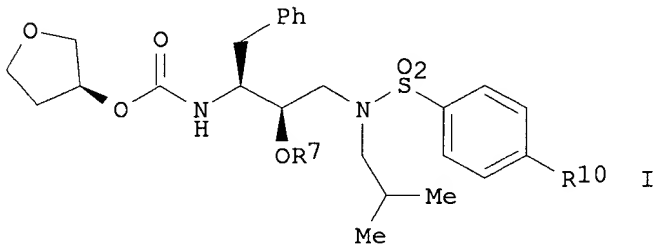
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933792	A2	19990708	WO 1998-US27403	19981223
WO 9933792	A3	19990916		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9920102	A1	19990719	AU 1999-20102	19981223

PRIORITY APPLN. INFO.: US 1997-68806P P 19971224
WO 1998-US27403 W 19981223
OTHER SOURCE(S): MARPAT 131:87803
GI



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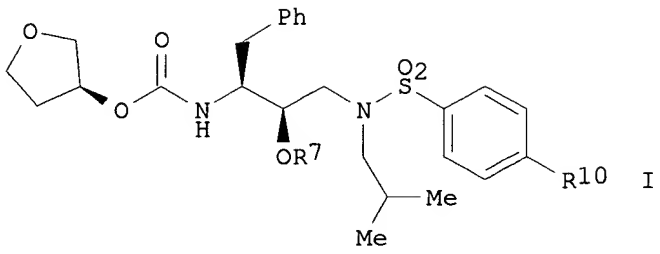

I

AB Z(CHD)pC(:G)(CXX1)mC(G1)N(D1)SO2E1 [Z = N(D)SO2E, NHA, NDA, NHE, NHCONDE, NH(Ht), Ht, ND(Ht); A = H, Ht, R1Ht, (substituted) R1Alk; Alk = alkyl, alkenyl; Ht = (substituted) cycloalkyl, cycloalkenyl, aryl, benzoheterocyclyl, heterocyclyl; D, D1 = R6, N(R2)2, (substituted) alkyl, alkenyl, cycloalkyl, etc.; E, E1 = Ht, OHt, HtHt, OR3, NR2R3, (substituted) alkyl, alkenyl; R1 = CO, SO2, COCO, O2C, OSO2, NR2CO, etc.; R2 = H, R6, R6-substituted alkyl; R3 = H, (substituted) Ht, alkyl, alkenyl; R6 = (substituted) aryl, carbocyclyl, heterocyclyl; G, G1 = H2, O; X, X1 = H, OH, NH2, SH, etc.; XX1 = O; m = 1-3; p = 0, 1], were prepd. Thus, title compd. (I; R7 = H; R10 = NO2) was heated with H3PO3 and DCC in pyridine to give 96% I (R7 = OP(O)(OH)H; R10 = NO2). This was heated with TMSOOTMS and (TMS)2NH to give 88% I (R7 = OP(O)(OH)2; R10 = NO2). The latter was hydrogenated and salified to give I (R7 = OP(O)(ONa)2; R10 = NH2) (II). II in a methylcellulose/EtOH/H2O formulation administered orally to dogs showed a relative availability of 60.4% relative to its metabolite VS-478.

L2 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:92655 CAPLUS

TITLE: The invention and development of CRIXIVAN An HIV protease inhibitor

AUTHOR(S): Dorsey, Bruce D.; Guare, James P., Jr.; Holloway, M. Katherine; Hungate, Randall W.; Vacca, Joseph P.

CORPORATE SOURCE: Department of Medicinal Chemistry, Merck Research Laboratories, West Point, PA, 19486, USA

SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), MEDI-142. American Chemical Society: Washington, D. C. CODEN: 67GHA6

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB The alarming spread of human immunodeficiency virus (HIV), the etiol. agent of the acquired immunodeficiency syndrome (**AIDS**), has initiated an urgent pursuit to comprehend and control this disease. Advances in mol., viral and cell biol. have defined numerous targets for potential drug intervention. The virally encoded homodimeric **aspartyl protease**, which is responsible for processing the gag and gag/pol gene products that allow for the organization of core structural proteins and release of viral enzymes, is one such target. Inhibition of this protease enzyme prevents the maturation and replication of the virus in cell culture. Recently, we and others have described antiviral effects of protease inhibitors in human clin. trials. These results confirm the importance of HIV protease (HIV-PR) inhibitors as another weapon in the arsenal needed to confront **AIDS**. We would like to report the discovery and development of a novel class of HIV-1 protease inhibitors which possess a high degree of intrinsic potency and inhibit the spread of the virus in infected cells at concns. of less than 100 nM. One of these inhibitors, L-735,524 (CRIXIVAN indinavir sulfate),

has shown excellent effects on surrogate markers, redn. in viral RNA and elevations of CD4 cells, in HIV infected patients. These results supported the rapid licensing of CRIXIVAN by FDA. The drug design rational, the development of the medicinal chem., and the presentation of human clin. results will be the focus of this lecture.

L2 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:9711 CAPLUS
DOCUMENT NUMBER: 130:71577
TITLE: Methods of increasing the bioavailability of stable crystal polymorphs of a compound
INVENTOR(S): Chaturvedi, Pravin Ramsewak; Boger, Joshua S.; Tung, Roger Dennis
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9857648	A1	19981223	WO 1998-US12474	19980616
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9881451	A1	19990104	AU 1998-81451	19980616

PRIORITY APPLN. INFO.: US 1997-876558 19970616
WO 1998-US12474 19980616

AB The present invention relates to methods of increasing the bioavailability of the most stable cryst. form of a compd., i.e. **aspartyl protease** inhibitor. The invention also relates to particles of the most stable cryst. form of a compd. having an av. particle size of less than 400 nm. The invention further relates to pharmaceutical compns. comprising these particles and the use of such pharmaceutical compns. for treating diseases, such as HIV. VX-478 polymorph Form V was subjected to wet milling in the presence of hydroxypropyl cellulose and sodium lauryl sulfate to have particles with a mean particle size of 157 nm. The particles were formulated into a suspension, which was administered to rats and pharmacokinetic studies were performed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:708925 CAPLUS
DOCUMENT NUMBER: 129:347287
TITLE: Nanosized **aspartyl protease** inhibitors
INVENTOR(S): Chaturvedi, Pravin Ramsewak; Tung, Roger Dennis; Boger, Joshua S.
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

09591464

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847492	A1	19981029	WO 1998-US7845	19980414
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9871338	A1	19981113	AU 1998-71338	19980414
PRIORITY APPLN. INFO.:			US 1997-844015	19970418
			WO 1998-US7845	19980414

AB The present invention relates to particles of the free base form of **aspartyl protease** inhibitors and pharmaceutical dosage forms contg. those particles. The invention also relates to methods of treating mammals with those pharmaceutical dosage forms.

L2 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:545376 CAPLUS
DOCUMENT NUMBER: 129:161492
TITLE: Preparation of 5,6-dihydropyrones as protease inhibitors and antiviral agents
INVENTOR(S): Ellsworth, Edmund Lee; Lunney, Elizabeth; Tait, Bradley Dean
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: U.S., 45 pp. Cont.-in-part of U. S. Ser. No. 155,443, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5789440	A	19980804	US 1994-319821	19941012
CA 2176041	AA	19950526	CA 1994-2176041	19941026
WO 9514011	A2	19950526	WO 1994-US12234	19941026
WO 9514011	A3	19950629		
W: AM, AU, BG, BY, CA, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LT, LV, MD, NO, NZ, PL, RO, RU, SI, SK, TJ, UA, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9480900	A1	19950606	AU 1994-80900	19941026
AU 680064	B2	19970717		
EP 729463	A1	19960904	EP 1994-932030	19941026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 75225	A2	19970428	HU 1996-1349	19941026
JP 09505292	T2	19970527	JP 1994-514454	19941026
RU 2160733	C2	20001220	RU 1996-113141	19941026
PL 180634	B1	20010330	PL 1994-314483	19941026
ZA 9409148	A	19950721	ZA 1994-9148	19941117
ZA 9409151	A	19950729	ZA 1994-9151	19941117
IL 111673	A1	19990411	IL 1994-111673	19941117
FI 9602021	A	19960712	FI 1996-2021	19960513

NO 9602018	A	19960704	NO 1996-2018		19960515
AU 9740974	A1	19980108	AU 1997-40974		19971013
AU 695088	B2	19980806			
US 5936128	A	19990810	US 1998-79689		19980515
PRIORITY APPLN. INFO.:			US 1993-155443	B2	19931119
			US 1993-155028	A	19931119
			US 1994-319768	A	19941012
			US 1994-319821	A	19941012
			WO 1994-US12234	W	19941026

OTHER SOURCE(S): MARPAT 129:161492

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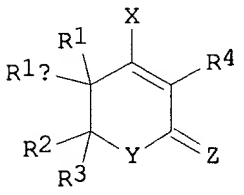

I

AB The title compds. [I; X = OR5, NHR5, CH2OR5, CO2R6, SR5 (wherein R5 = R6, COR6; R6 = H, C1-6 alkyl, C3-7 cycloalkyl, etc.); Z = O, S; Y = O, S; R1, R1a = (CH2)n1(W1)n2(AR)n2(CH2)n3(W2)n4R7; R2, R3 is selected from the group of structures from which R1 is selected with the proviso that if W1 is a heteroatom n1 = 1-4; R2R3 = (un)substituted 3-7 membered ring; R4 = (W3)(CH2)n3(W4)n4(Ar)n2(CH2)n3(W2)n4R7; n1 = 0-4; n2 = 0-1; n3 = 0-4; n4 = 0-1; n5 = 0-2; W1, W2, W4 = O, CO, C.tplbond.C, etc.; W3 = O, OC(O), NR7, etc.; R7 = H, Ar, C1-6 alkyl, etc.; Ar = (un)substituted Ph, naphthyl, 5-6 membered heterocyclyl contg. 1-4 heteroatoms, etc.], which potently inhibit the HIV **aspartyl protease** blocking HIV infectivity and are useful in the development of therapies for the treatment of bacterial and viral infections and diseases, including **AIDS**, were prepd. Thus, reaction of 5,6-dihydro-4-hydroxy-6-phenyl-2H-pyran-2-one with 2-phenylethyl p-toluenethiosulfonate in the presence of Et3N in EtOH afforded I [X = OH; Y = O; Z = O; R1, R1a, R2 = H; R3 = Ph; R4 = (2-phenylethyl)thio] which showed IC50 of 1.9 .mu.M against HIV protease.

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 25	Searching with the P indicator for Preparations
NEWS 4	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 5	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 6	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 7	Mar 08	Gene Names now available in BIOSIS
NEWS 8	Mar 22	TOXLIT no longer available
NEWS 9	Mar 22	TRCTHERMO no longer available
NEWS 10	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 11	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:17:21 ON 02 APR 2002

09591464

STRUCTURE FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6
DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

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=> s asparyl protease
             0 ASPARYL
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L1           0 ASPARYL PROTEASE
                 (ASPARYL(W)PROTEASE)

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                8.38       8.59

FILE 'CAPLUS' ENTERED AT 09:17:41 ON 02 APR 2002
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09591464

FILE COVERS 1907 - 2 Apr 2002 VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002 (20020330/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

```
=> s aspartyl  protease
          4023 ASPARTYL
         68986 PROTEASE
L2         394 ASPARTYL  PROTEASE
                (ASPARTYL(W)PROTEASE)

=> s l2 and hiv
         42962 HIV
L3         118 L2 AND HIV

=> d l3 1-10 ibib abs hitstr
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L3 ANSWER 1 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:935058 CAPLUS
TITLE: Human immunodeficiency virus and host cell lipids. Interesting pathways in research for a new **HIV** therapy
AUTHOR(S): Raulin, Jeanine
CORPORATE SOURCE: Universite Denis Diderot, Paris, 75251, Fr.
SOURCE: Progress in Lipid Research (2001), Volume Date 2002, 41(1), 27-65
CODEN: PLIRDW; ISSN: 0163-7827
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been reported in the literature that biol. membranes arising from **HIV**-induced cell fusion, as well as syncytium formation between infected and non-infected cells and those involved in transduction, viral DNA nuclear import and virion budding from the host cell, are all made of proteins, a phospholipid (P) bilayer and cholesterol (C). However, the P/C molar ratio is higher in the retroviral envelope than in the plasma membrane where they originate, and higher than in the nuclear envelope. Mechanisms are described which elucidate this puzzling fact, as well as cholesterol-dependent leakage and pore formation during cell fusion. Fatty acylation of viral and host cell proteins is required to direct them to membranes. Detergent-insol. microdomains enriched in cholesterol and sphingolipids, termed either DIGs (detergent-insol. glycolipid-enriched complexes), DRMs (detergent resistant membranes), TIFFs (Triton-insol. floating fractions) or GEMs (glycolipid-enriched membranes), function as platforms for attachment of proteins in the process of signal transduction. **HIV**-SUgp120 (**HIV**-surface glycoprotein),

T-cell receptor (TCR)-CD4+ and co-receptors promote aggregation of these lipid "rafts" which conc. the Src family tyrosine kinases SFKs (PTK, Lyn, Fyn, Lck), GPI (glycosyl phosphatidylinositol)-anchored proteins, and phosphatidylinositol kinases PI(3)K and PI(4)K, inducing cell signalling. **HIV**-SUgp120 transduces the activation signal and provokes the formation of polyunsatd. fatty acid (PUFA) metabolites, i.e. the prostaglandin PGE2 suppressor of immune function and inhibitor of cytotoxic T-lymphocyte (CTL) proliferation, while PGB2 activates SFKs and increases mRNA expression, as well as NF.kappa.B (nuclear transcription factor) translocation to nucleus. **HIV** nuclear import, DNA integration, chromatin template capacity may be mediated by the lipid environment. The lipid-enriched microdomains from which **HIV**-1 buds, may explain the high level of cholesterol and sphingolipids in the viral envelope, since host cell rafts become a viral coat. **HIV** -1 infection induces alteration of cellular lipids: (1) shift in phospholipid synthesis to neutral lipids assocd. with the viral load, polyunsatd. fatty acid (PUFA) peroxidn., and n-3 deficiency with deregulation of cytokines and PPAR-.gamma. (peroxisome proliferator-activated receptor-.gamma.), and (2) alloimmune phospholipid antibody prodn. in which antibodies to cardiolipin and to phosphatidylserine are most prevalent, due to the destruction of mitochondrial membranes and progression of lymphocyte apoptosis. The current highly active anti-retroviral therapy, including both viral reverse transcriptase (RT) inhibitors (NRTIs and NNRTIs, nucleoside and non-nucleoside RT inhibitors) and protease inhibitors (PIs), induces side-effects in the long term. Lipodystrophy (LD), consists of peripheral lipoatrophy assocd. with central fat accumulation (called "crixbelly" and "buffalo hump"), insulin resistance, elevation of very low d. lipoproteins, decrease in high d. lipoproteins and inhibition of adipocyte differentiation. LD syndrome appears to be induced by PIs that inhibit GLUT4, glucose transporter isoform, and by NRTIs which provoke mitochondrial failure. New therapeutic strategies assessed: (1) inhibition of the viral integrase and/or **HIV** entry into cells through natural products or their derivs., (2) inhibition of **HIV** -1 entry into macrophages pretreated with Gram-neg. bacterial lipopolysaccharide, (3) vaccination with multi-lipopeptides, i.e. sequences of **HIV**-1 peptides with CD4+ T-cell and B-cell epitopes, modified by adding a lipid tail to one end, which produce **HIV**-specific CTL and multispecific immune responses in most of the vaccinated subjects and (4) stimulation of antiviral drug activity with lipid-prodrugs targeting viral RT, polymerase, integrase, or **aspartyl-protease**.

REFERENCE COUNT: 217 THERE ARE 217 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:879508 CAPLUS
TITLE: Syntheses of FDA approved **HIV** protease inhibitors
AUTHOR(S): Ghosh, Arun K.; Bilcer, Geoffrey; Schiltz, Gary
CORPORATE SOURCE: Department of Chemistry, University of Illinois at Chicago, Chicago, IL, 60607, USA
SOURCE: Synthesis (2001), (15), 2203-2229
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The treatment of **HIV** and AIDS was revolutionized by the introduction of peptidomimetic **aspartyl protease**

inhibitors. One of the major limitations of this type of therapy is that higher therapeutic doses are necessary because of the presence of "peptide-like" features in the drugs. Therefore, adequate supplies and cost effective syntheses of these drugs are of utmost importance. To date, there are six protease inhibitors approved by the United States Food and Drug Administration (FDA) for the treatment of **HIV** and AIDS. This review focuses on the published syntheses of currently FDA approved **HIV** protease inhibitor drugs, their isosteres and ligands.

REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

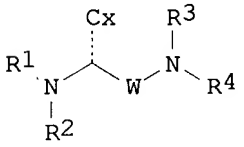
L3 ANSWER 3 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693271 CAPLUS
DOCUMENT NUMBER: 135:227248
TITLE: Preparation of amino acid derivatives as **HIV** **aspartyl protease** inhibitors
INVENTOR(S): Stranix, Brent Richard; Sauve, Gilles; Bouzide, Abderrahim; Sevigny, Guy; Yelle, Jocelyn
PATENT ASSIGNEE(S): Pharmacor Inc., Can.
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068593	A2	20010920	WO 2001-CA296	20010307
WO 2001068593	A3	20020228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-526209 A 20000315
OTHER SOURCE(S): MARPAT 135:227248
GI



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AB The invention relates to a class of amino acid derivs. I [W = (CH2)n or CH2-XX-CH2CH2, where n = 1-5, XX = O, NR5 (R5 = H, alkyl), S, SO, SO2; Cx = CO2M (M is an alkali or alk. earth metal), CO2R5, CH2OH, CONR5R6 (R6 = H, alkyl), CONHOH, Fmoc-Lys-NHCO (Fmoc = 9-fluorenylmethoxycarbonyl), benzyloxycarbonyl or tetrazolyl; R1, R3 = H, Me3O2C, alkyl,

cycloalkylalkyl, arylalkyl or heterocyclylalkyl having a defined structure; R2, R4 = H, CHO, CF3, acyl or sulfonyl groups (e.g., 4-PhCH2CH2CONHC6H4SO2, camphor-10-CH2SO2, naphthyl-SO2, fluorenyl-SO2, and quinoline-SO2), arylalkyl of defined structure] or pharmaceutically acceptable ammonium salts having **HIV aspartyl protease** inhibitory properties. Thus, N.alpha.-isobutyl-N.alpha.-tosyl-N.epsilon.-Fmoc-L-lysine (II) was prepd. from N.epsilon.-benzyloxycarbonyl-L-lysine benzyl ester by N-alkylation using isobutyraldehyde, N-tosylation, hydrogenolysis, and protection with Fmoc-O-succinimide. Compd. II showed Ki = 4.3 nM for inhibition of **HIV aspartyl protease**.

L3 ANSWER 4 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:674667 CAPLUS
DOCUMENT NUMBER: 135:338662
TITLE: Pharmacokinetics and design of **aspartyl protease** inhibitors
AUTHOR(S): Thompson, Lorin A.; Tebben, Andrew J.
CORPORATE SOURCE: DuPont Pharmaceuticals Company, Wilmington, DE, 19880, USA
SOURCE: Annual Reports in Medicinal Chemistry (2001), 36, 247-256
CODEN: ARMCBI; ISSN: 0065-7743
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 80 refs., summarizes recent work to develop superior second-generation **HIV** protease inhibitors, focusing on improvements in the pharmacokinetics and dosing schedules of current clin. candidates. It highlights recent progress toward the clin. evaluation of nonpeptidic inhibitors of renin. Efforts to improve computational tools and methods useful for inhibitor design are discussed. (c) 2001 Academic Press.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:501832 CAPLUS
DOCUMENT NUMBER: 135:242488
TITLE: Analysis of amide bond formation with an .alpha.-hydroxy-.beta.-amino acid derivative, 3-amino-2-hydroxy-4-phenylbutanoic acid, as an acyl component: byproduction of homobislactone
AUTHOR(S): Hayashi, Yoshio; Kinoshita, Yuko; Hidaka, Koushi; Kiso, Aiko; Uchibori, Hirokazu; Kimura, Tooru; Kiso, Yoshiaki
CORPORATE SOURCE: Department of Medicinal Chemistry Center for Frontier Research in Medicinal Science, Kyoto Pharmaceutical University, Yamashina-Ku, Kyoto, 607-8412, Japan
SOURCE: Journal of Organic Chemistry (2001), 66(16), 5537-5544
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the synthesis of peptidomimetics contg. .alpha.-hydroxy-.beta.-amino acid, the coupling of this N.beta.-protected .beta.-amino acid with amine components was generally performed without the protection of its .alpha.-hydroxyl group. However, the formation of dipeptides in low yield was often obsd. when sterically hindered amine components were used. Boc-Apns-OH [Apns: (2S,3S)-3-amino-2-hydroxy-4-phenylbutanoic acid,

allophenylnorstatine] (6), which is one of such .beta.-amino acid derivs., is intensively employed as a core structure in the development of **HIV**-1 protease inhibitors. There have been no precise studies, to date, that have examd. amide bond formation with .alpha.-hydroxy-.beta.-amino acid derivs. as an acyl component. To det. the cause of this low-yield reaction, we studied the amide bond formation focusing on the activation step of N.beta.-protected .alpha.-hydroxy-.beta.-amino acid by using a model coupling reaction between 6 and H-Dmt-OR [Dmt: (R)-5,5-dimethyl-1,3-thiazolidine-4-carboxylic acid] (7). A significant amt. of homobislactone was formed through the activation of the carboxyl group of 6 to the benzotriazole-type active esters such as OBt and OAt. In addn., this homobislactone formation was markedly increased in the presence of a catalytic amt. of a base, which exhibited good correlation with the low yield of the amide bond formation, suggesting that homobislactone formation is one major reason for the low yield of the amide bond formation. Moreover, homobislactones were also formed in other derivs. of the N.beta.-protected .alpha.-hydroxy-.beta.-amino acid, suggesting a common feature of this type of amino acids. The use of a strong activation method like EDC-HOAt without base addn. enhanced amide bond formation, although a small amt. of homobislactone may be formed during the coupling reaction.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:91617 CAPLUS
DOCUMENT NUMBER: 134:231442
TITLE: Improved scoring of ligand-protein interactions using OWFEG free energy grids
AUTHOR(S): Pearlman, David A.; Charifson, Paul S.
CORPORATE SOURCE: Vertex Pharmaceuticals Incorporated, Cambridge, MA, 02139-4242, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(4), 502-511
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new approach to rapidly score protein-ligand interactions is tested on several protein-ligand systems. Results using this approach - the OWFEG free energy grid - are quite promising and are generally in better agreement with expt. (in some cases much better) than those obtained employing scoring techniques currently in wide use. The OWFEG free energy grid is generated from a one-window free energy perturbation MD simulation (Pearlman, D. A. J. Med. Chem. 1999, 42, 4313-4324). The OWFEG approach is applied to three protein systems: IMPDH, MAP kinase p38, and **HIV**-1 **aspartyl protease**. OWFEG scores are compared to exptl. Ki and IC50 data in each case. Empirical scoring functions applied to the same systems for comparison include ChemScore, Piecewise Linear Potential (PLP), and Dock energy score.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:900607 CAPLUS
DOCUMENT NUMBER: 134:56676
TITLE: Preparation of arylsulfonamides as inhibitors of **aspartyl protease**
INVENTOR(S): Hale, Michael Robin; Tung, Roger; Price, Stephen; Wilkes, Robin David; Schairer, Wayne Carl; Jarvis, Ashley Nicholas; Spaltenstein, Andrew; Furfine, Eric

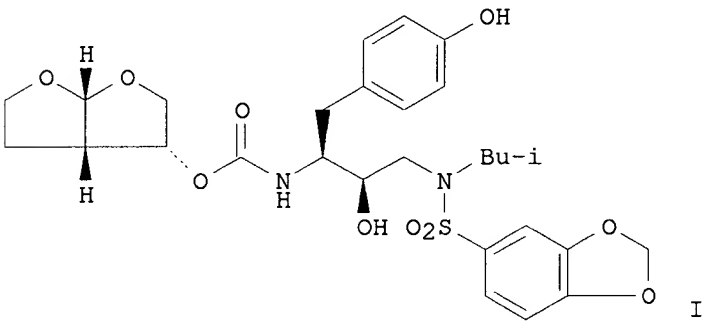
09591464

Steven; Samano, Vicente; Kaldor, Istvan; Miller, John Franklin; Brieger, Michael Stephen
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Inc., USA; et al.
SOURCE: PCT Int. Appl., 396 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076961	A1	20001221	WO 2000-US15781	20000608
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NO 2001006034	A	20020118	NO 2001-6034	20011210

PRIORITY APPLN. INFO.: US 1999-139070P P 19990611
US 2000-190211P P 20000317
WO 2000-US15781 W 20000608

OTHER SOURCE(S): MARPAT 134:56676
GI



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AB The title arylsulfonamides, namely (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 3-arylsulfonylamino-1-(4-hydroxyphenyl)-2-hydroxypropylcarbamate derivs. (e.g. I) are prepd. These compds. are particularly well suited for inhibiting **HIV**-1 and **HIV**-2 protease activity and consequently, may be advantageously used as anti-viral agents against the **HIV**-1 and **HIV**-2 viruses. They are useful for treating with a patient diagnosed with AIDS, AIDS related complex (ARC), progressive generalized lymphadenopathy (PGL), Kaposi's sarcoma, thrombocytopenic purpura, or AIDS-related neurol. conditions such as AIDS dementia complex, multiple sclerosis or tropical paraperesis, etc. Thus, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 3-[N-(1,3-benzodioxol-5-ylsulfonyl)-N-isobutylamino]-1-(4-hydroxyphenyl)-2-hydroxypropylcarbamate underwent Mitsunobu reaction with phenethyl alc. using Ph3P and di-tert-Bu azodicarbonate in CH2Cl2 at room temp. for 1.5 h to give 72% I. I showed IC50 of <0.001, <0.001, and 0.01-0.001 .mu.M against drug-resistant **HIV** strains, i.e. wild type, mutant **HIV**-1 EP13, and

mutant D545701-14 **HIV** strains, resp., in MT-4 cells.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:857874 CAPLUS
DOCUMENT NUMBER: 134:174581
TITLE: Modulation of protease activity by NO-mediated S-nitrosylation
AUTHOR(S): Ascenzi, Paolo; Colasanti, Marco; Persichini, Tiziana; Polticelli, Fabio; Venturini, Giorgio; Bortolotti, Fabrizio; Menegatti, Enea
CORPORATE SOURCE: Department of Biology, University of Rome "Tre", Rome, I-00146, Italy
SOURCE: Current Topics in Peptide & Protein Research (1999), 3, 181-188
CODEN: CTPPFA
PUBLISHER: Research Trends
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 36 refs. Nitric oxide (NO) is generated in different cell types by the concomitant conversion of L-arginine into L-citrulline through the enzyme NO synthase. NO has been claimed to exert its action in an increasing no. of physiol. and pathol. events. Among others, cellular communication, blood pressure regulation, homeostasis and memory formation. A huge amt. of NO is also produced under pathol. conditions, such as inflammation and immunol. processes. This wide variety of effects is achieved through interactions of NO with some targets via a rich redox and additive chem. In particular, it has been shown that NO-mediated S-nitrosylation inhibits the activity of several enzymes, contg. Cys residue(s) at their catalytic site, e.g. papain, caspases and cathepsin-B. Moreover, NO may modulate the activity of enzymes contg. Cys residues at their regulatory regions. In this respect, NO-mediated S-nitrosylation of the regulatory Cys residues inactivates the viral-encoded **aspartyl protease**, a crucial enzyme for **HIV**-1 replication. Finally, the NO-mediated S-nitrosylation of Cys83, the single free sulfhydryl residue present in the fibronectin type-1 and epidermal growth factor-like pair of modules of the tissue-type plasminogen activator (t-PA) does not affect the catalytic (i.e. fibrinolytic) activity, but endows the serine protease with new potent vasodilatory and antiplatelet properties. In this respect, t-PA acts as a macromol. NO-transporter. Here, the NO-mediated S-nitrosylation of some representative proteases is reviewed.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:790450 CAPLUS
DOCUMENT NUMBER: 133:335432
TITLE: Preparation of D-mannitol derivatives as **HIV aspartyl protease** inhibitors
INVENTOR(S): Sauve, Gilles; Bouzide, Abderrahim
PATENT ASSIGNEE(S): Pharmacor Inc., Can.
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066524	A1	20001109	WO 2000-CA484	20000427
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6313177	B1	20011106	US 1999-302185	19990430
EP 1175385	A1	20020130	EP 2000-922387	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-302185 A 19990430
WO 2000-CA484 W 20000427

OTHER SOURCE(S): MARPAT 133:335432

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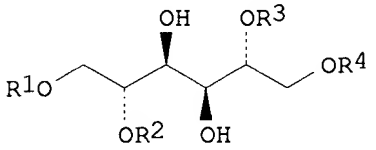

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AB A D-mannitol deriv. selected from the group consisting of a compd. of formula I pharmaceutically acceptable derivs. thereof and where applicable or appropriate pharmaceutically acceptable salts thereof, wherein R1-R4 are the same or different and may, for example, each independently be selected from among alkyl, benzyl, substituted benzyl, and aryl (i.e. arom. including arom. like) groups. The D-mannitol derivs. may be used as **HIV aspartyl protease** inhibitors. Thus, 1,2,5,6-tetra-O-benzyl-D-mannitol was prepd. and tested as as **HIV aspartyl protease** inhibitor (Ki = 2.0 .mu.M).

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:699185 CAPLUS
DOCUMENT NUMBER: 133:267150
TITLE: Preparation of amino acid sulfonamide derivatives as inhibitors of **aspartyl protease**
INVENTOR(S): Tung, Roger Dennis; Salituro, Francesco Gerald; Deininger, David D.; Murcko, Mark Andrew; Novak, Perry Michael; Bhisetti, Govinda Rao
PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Incorporated, USA
SOURCE: U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 207,580, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6127372	A	20001003	US 1996-424372	19960401
WO 9524385	A1	19950914	WO 1995-US2420	19950224

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1994-207580 B2 19940307
WO 1995-US2420 W 19950224

OTHER SOURCE(S): MARPAT 133:267150

AB Sulfonamides Z-(CH-D)pC(:G)(CXX')mC(:G')N(D')SO2-E' [Z = N(D), SO2E, NH-A, N(D)-A, NH-E, NHC(O)N(D)(E), NH-Ht, N(D)-Ht or phthalimidyl (A = Ht or -R1-Ht, where Ht is a heterocycle which may be substituted, R1 = CO, SO2, COCO, O2C, OSO2, NHSO2, NHCO, NHCOCO, which may be substituted); D, D' = aryl, carbocycle, Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl, etc.; m = 1-3; p = 0 or 1; G, G' = H2 or O; X, X' = H, OH, NH2, SH, D, halo or XX' = O] were prepd. as **aspartyl protease** inhibitors. Thus, t-BuNHCON(CH2Ph)CH2CH(OH)N(CH2-cyclopentyl)SO2C6H4OMe-p, prepd. by sequential reactions of cyclopentylmethylamine, p-methoxybenzenesulfonyl chloride, epibromohydrin, benzylamine, and t-Bu isocyanate, showed Ki = 2,400 for inhibition of **HIV**-1 protease.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l3 111-118 ibib abs hitstr

L3 ANSWER 111 OF 118 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:424678 CAPLUS
DOCUMENT NUMBER: 115:24678
TITLE: Effect of pepstatin A on structure and polymerization of intermediate filament subunit proteins in vitro
AUTHOR(S): Mothes, Elfriede; Shoeman, Robert L.; Traub, Peter
CORPORATE SOURCE: Max-Planck-Inst. Zellbiol., Ladenburg, D-6802, Fed. Rep. Ger.
SOURCE: J. Struct. Biol. (1991), 106(1), 64-72
CODEN: JSBIEM; ISSN: 1047-8477
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pepstatin A, a pentapeptide **aspartyl protease** inhibitor, can interact with intermediate filament (IF) subunit proteins and induce their polymn. in the absence of salt into long filaments with a rough surface and a diam. of 15-17 nm. This polymn. appears to be driven primarily by non-ionic interactions between pepstatin A and polymn.-competent forms of IF proteins, resulting in a composite filament. Proteolytic fragments of vimentin, lacking portions of only the head domain or of both the head and tail domains, failed to copolymerize with pepstatin A into long filaments under these conditions. Rather, these peptides, as well as control proteins like bovine serum albumin, were found to decorate pepstatin A polymers (filaments, ribbons, and sheets) by sticking to their surfaces. In addn. to the electron microscopy expts., UV difference spectra, ultracentrifugation, and SDS-PAGE anal. of in vitro cleavage products of vimentin obtained with **HIV**-1 protease all provided independent evidence for a direct assocn. of pepstatin A and IF subunit proteins, with subsequent alterations in the IF subunit protein conformation. These data show that non-ionic interactions can substitute for the effect of salt and effectively drive the higher-order polymn. of

IF subunit proteins.

L3 ANSWER 112 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:224356 CAPLUS
DOCUMENT NUMBER: 114:224356
TITLE: Polymerizing properties of pepstatin A
AUTHOR(S): Mothes, Elfriede; Shoeman, Robert L.; Schroeder, Rasmus R.; Traub, Peter
CORPORATE SOURCE: Max-Planck-Inst. Zelbiol., Ladenburg/Heidelberg, D-6802, Fed. Rep. Ger.
SOURCE: J. Struct. Biol. (1990), 105(1-3), 80-91
CODEN: JSBIEM; ISSN: 1047-8477
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pepstatin A, a pentapeptide **aspartyl protease** inhibitor, can spontaneously polymerize into filaments having a helical substructure and, after neg. staining, characteristic diams. ranging from 6 to 12 nm. Optical diffraction anal. demonstrated that these filaments consist of a 6-nm-wide strand helically wound with a periodic pitch of 25 nm. Selected images suggest that these filaments may actually be composed of two, intertwined 6-nm-wide strands, an hypothesis not at variance with the diffraction data. These filaments may extend over several micrometers. At low ionic strength and neutral pH, the crit. concn. for pepstatin A filament assembly is 0.1 mM. At higher pepstatin A concns. or in physiol. salt solns., a variety of higher-order structures were obsd., including ribbons, sheets, and cylinders with both regular and twisted or irregular geometries. Pepstatin A polymd. into these higher-order structures loses its ability to inhibit the **aspartyl protease** of the human immunodeficiency virus type 1. These results have implications not only for model studies on the polymn. of small peptides into higher-order structures, but also for the practical development of sol. protease inhibitors.

L3 ANSWER 113 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:199055 CAPLUS
DOCUMENT NUMBER: 114:199055
TITLE: Design, structure-activity and specificity of highly potent P1-P'1-modified pseudopeptidyl inhibitors of **HIV**-1 **aspartyl protease**
AUTHOR(S): Sawyer, Tomi K.; Tomasselli, Alfredo G.; Poorman, Roger A.; Hui, John O.; Hinzmann, Jessica; Staples, Douglas J.; Maggiora, Linda L.; Smith, Clark W.; Heinrikson, R.
CORPORATE SOURCE: Biopolym. Chem. Unit, Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 11th (1990), Meeting Date 1989, 855-7. Editor(s): Rivier, Jean E.; Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.
CODEN: 56XTA7
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A discussion in which the recombinant **HIV**-1 **aspartyl protease** inhibition by pepstatin and GAG228-135-based octapeptide derivs. is described. U-85548E is the first reported **HIV** substrate-based inhibitor having a Leu .psi. [CH(OH)CH2]Val moiety at the P, -P', site. Structure-activity and specificity are discussed.

L3 ANSWER 114 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:117316 CAPLUS

09591464

DOCUMENT NUMBER: 114:117316
TITLE: Microbore liquid chromatography coupled to a flow fast atom bombardment probe for the on-line detection of the Tyr-Pro cleavage of a nonapeptide by recombinant **HIV**-1 protease
AUTHOR(S): Cole, S. M.; Macrae, P. V.; Merson, J. R.; Pullen, F. S.; Rance, D. J.
CORPORATE SOURCE: Pfizer Cent. Res., Sandwich/Kent, CT13 6NJ, UK
SOURCE: J. Chromatogr. (1991), 562(1-2), 67-72
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The nonapeptide Val-Ser-Gln-Asn-Tyr-Pro-Ile-Val-Gln has been reported as a model substrate for an **aspartyl protease** produced by the human immunodeficiency virus (**HIV**-1). Cleavage of this peptide at the Tyr-Pro linkage to produce tetra- and pentapeptide fragments is the basis of HPLC assays to detect **HIV**-1 protease activity. Confirmation of the cleavage site has been proved by using microbore chromatog. coupled to a dynamic fast atom bombardment interface. Comparison with fortified control indicates that an approx. stoichiometric amt. of the tetrapeptide was formed from the nonapeptide, confirming that the cleavage of the substrate by **HIV**-1 protease is both specific and quant.

L3 ANSWER 115 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:58080 CAPLUS
DOCUMENT NUMBER: 114:58080
TITLE: Characterization of an active single polypeptide form of the human immunodeficiency virus type 1 protease
AUTHOR(S): DiIanni, Carolyn L.; Davis, Lenora J.; Holloway, M. Katharine; Herber, Wayne K.; Darke, Paul L.; Kohl, Nancy E.; Dixon, Richard A. F.
CORPORATE SOURCE: Dep. Mol. Biol., Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: J. Biol. Chem. (1990), 265(28), 17348-54
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pepsin-like aspartyl proteases consist of a single polypeptide chain with topol. similar N- and C-terminal domains, each of which contributes 1 aspartic acid residue to the active site. This structure has been proposed to have evolved by gene duplication and fusion from a dimeric enzyme composed of two identical polypeptide chains, such as the **aspartyl protease** (PRT) of human immunodeficiency virus type 1 (**HIV**-1). To det. if a single polypeptide form of the **HIV**-1 protease would be enzymically active, two protease coding regions were linked to form a dimeric gene (pFGGP). Expression of this gene in Escherichia coli yielded a protein with the expected mol. mass of 22 kDa. The in vitro kinetic parameters of PRT and FGGP (where FGGP is the single polypeptide form of the **HIV**-1 protease with 2 glycine residues connecting the two subunits) for three peptide substrates are similar. Construction and anal. of a CheY-GAG-FGGP fusion protein demonstrated that FGGP is capable of precursor processing in vivo. Mutation of one or both of the active site aspartates to either asparagine or glutamate rendered the enzyme inactive, demonstrating that both active site aspartate residues are required for enzymic activity.

L3 ANSWER 116 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:38825 CAPLUS
DOCUMENT NUMBER: 114:38825

09591464

TITLE: Human immunodeficiency virus protease: a target for AIDS therapy
AUTHOR(S): Debouck, Christine; Metcalf, Brian W.
CORPORATE SOURCE: Dep. Mol. Genet., SmithKline Beecham Pharm., King of Prussia, PA, 19406, USA
SOURCE: Drug Dev. Res. (1990), 21(1), 1-17
CODEN: DDREDK; ISSN: 0272-4391
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 114 refs. of inhibitors blocking viral protease in **HIV**-infected cells and impairing the viral life cycle. Other approaches to interfere with viral protease activity or prodn. are also discussed.

L3 ANSWER 117 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:419806 CAPLUS
DOCUMENT NUMBER: 113:19806
TITLE: Fluorescence-based continuous assay for the **aspartyl protease** of human immunodeficiency virus-1
AUTHOR(S): Geoghegan, Kieran F.; Spencer, Robin W.; Danley, Dennis E.; Contillo, Leonard G., Jr.; Andrews, Glenn C.
CORPORATE SOURCE: Pfizer Cent. Res., Groton, CT, 06340, USA
SOURCE: FEBS Lett. (1990), 262(1), 119-22
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5-Dimethylaminonaphthalene-1-sulfonyl-Ser-Gln-Asn-Tyr-Pro-Ile-Val-Trp (Dns-SQNYPIVW) is a fluorescent substrate for the **aspartyl protease** of human immunodeficiency virus-1. In intact substrate, fluorescence of tryptophan (Trp) (.lambda.ex 290 nm, .lambda.em 360 nm) was 60% quenched by energy transfer to the dansyl group. Protease-catalyzed cleavage at the Tyr-Pro bond abolished the energy transfer, and the consequent increase in Trp fluorescence was used to follow the enzymic reaction. At substrate concns. <60 .mu.M, initial reaction velocity increased as a linear function of substrate concn., with kcat/KM = 9700 M-1 s-1. Limited soly. and internal fluorescence quenching precluded a detn. of KM for Dns-SQNYPIVW, but this was clearly >100 .mu.M.

L3 ANSWER 118 OF 118 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:169225 CAPLUS
DOCUMENT NUMBER: 110:169225
TITLE: Three-dimensional structure of **aspartyl protease** from human immunodeficiency virus **HIV**-1
AUTHOR(S): Navia, Manuel A.; Fitzgerald, Paula M. D.; McKeever, Brian M.; Leu, Chih Tai; Heimbach, Jill C.; Herber, Wayne K.; Sigal, Irving S.; Darke, Paul L.; Springer, James P.
CORPORATE SOURCE: Dep. Biophys. Chem., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Nature (London) (1989), 337(6208), 615-20
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal structure of the protease of the human immunodeficiency virus type 1 (**HIV**-1), which releases structural proteins and enzymes from viral polyprotein products, has been detd. to 3 .ANG. resoln. Large regions of the protease dimer, including the active site, have structural

homol. to the family of microbial aspartyl proteases. The structure suggests a mechanism for the autoproteolytic release of protease and a role in the control of virus maturation.

09591464

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS 3	Jan 25	Searching with the P indicator for Preparations
NEWS 4	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS 5	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS 6	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS 7	Mar 08	Gene Names now available in BIOSIS
NEWS 8	Mar 22	TOXLIT no longer available
NEWS 9	Mar 22	TRCTHERMO no longer available
NEWS 10	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS 11	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 09:21:17 ON 02 APR 2002

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:21:24 ON 02 APR 2002

09591464

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6
DICTIONARY FILE UPDATES: 31 MAR 2002 HIGHEST RN 403640-18-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

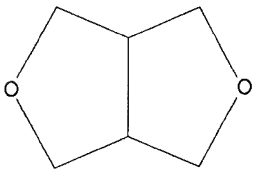
The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved. Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies. Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

=>
Uploading 591464b.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 09:21:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 304 TO ITERATE

100.0% PROCESSED 304 ITERATIONS 50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

09591464

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5034 TO 7126
PROJECTED ANSWERS: 833 TO 1807

L2 50 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 09:21:47 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6224 TO ITERATE

100.0% PROCESSED 6224 ITERATIONS 1393 ANSWERS
SEARCH TIME: 00.00.01

L3 1393 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 140.28 140.49

FILE 'CAPLUS' ENTERED AT 09:21:51 ON 02 APR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 2 Apr 2002 VOL 136 ISS 14
FILE LAST UPDATED: 30 Mar 2002 (20020330/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> s l3 and aids?
1778 L3
40954 AIDS?

09591464

L4 5 L3 AND AIDS?

=> d l4 1-5 ibib abs hitstr

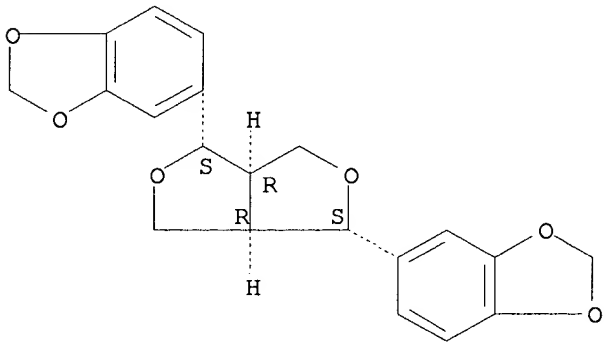
L4 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:893127 CAPLUS
DOCUMENT NUMBER: 134:290169
TITLE: New constituents and antiplatelet aggregation and anti-HIV principles of Artemisia capillaris
AUTHOR(S): Wu, T.-S.; Tsang, Z.-J.; Wu, P.-L.; Lin, F.-W.; Li, C.-Y.; Teng, C.-M.; Lee, K.-H.
CORPORATE SOURCE: Department of Chemistry, National Cheng Kung University, Tainan, Taiwan
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(1), 77-83
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five new constituents including a flavonoid, artemisidin A (1), and four coumarins, artemicapin A, artemicapin B, artemicapin C and artemicapin D together with 70 known compds., have been isolated and characterized from the aerial part of Artemisia capillaris. The structures of these compds. were detd. from spectral analyses and/or chem. evidence. Among them, some of compds. showed antiplatelet aggregation activity and some compds. demonstrated significant activity against HIV replication in H9 lymphocytic cells.

IT **607-80-7P**, (+)-Sesamin **28168-96-9P**, Pluviatide
RL: PUR (Purification or recovery); PREP (Preparation)
(antiplatelet aggregation, anti-HIV effect and isolation and characterization of flavonoids from aerial part of Artemisia capillaris)

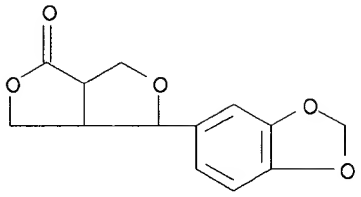
RN 607-80-7 CAPLUS
CN 1,3-Benzodioxole, 5,5'-(tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl)bis-, (1S,3aR,4S,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



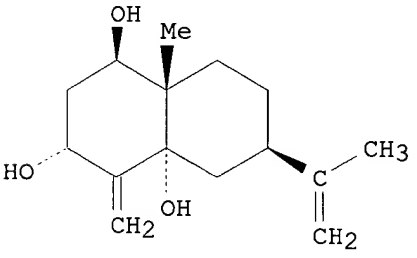
RN 28168-96-9 CAPLUS
CN 1H,3H-Furo[3,4-c]furan-1-one, 4-(1,3-benzodioxol-5-yl)tetrahydro- (9CI) (CA INDEX NAME)

09591464

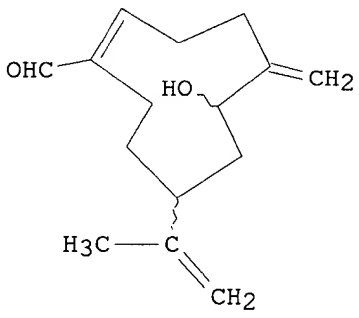


REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:792843 CAPLUS
DOCUMENT NUMBER: 134:68789
TITLE: Anti-HIV agents 45 and antitumor agents 205. Two new sesquiterpenes, leitneridanins A and B, and the cytotoxic and anti-HIV principles from Leitneria floridana
AUTHOR(S): Xu, Zhihong; Chang, Fang-Rong; Wang, Hui-Kang; Kashiwada, Yoshiki; McPhail, Andrew T.; Bastow, Kenneth F.; Tachibana, Yoko; Cosentino, Mark; Lee, Kuo-Hsiung
CORPORATE SOURCE: Natural Products Laboratory Division of Medicinal Chemistry and Natural Products School of Pharmacy, University of North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Journal of Natural Products (2000), 63(12), 1712-1715
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB Two new sesquiterpenes, leitneridanin A (I) and leitneridanin B (II), and seven known compds., lirioresinol B, (-)-pinoresinal, (+)-lariciresinol, quassimarin (III), simalikalactone D (IV), 1-methoxycanthinone (V), and 5-methoxycanthinone (VI), were isolated from Leitneria floridana. Their structures were identified on the basis of spectral data. In vitro biol. evaluation showed that V is a potent anti-HIV agent (EC50 0.26 .mu.g/mL; TI >39) and that III-VI suppressed the growth of a panel of human tumor cell lines (KB, A-549, HCT-8, CAKI-1, MCF-7, and SK-MEL-2). Compds. III and IV were significantly active, with ED50 values in the range of 0.26-0.012 .mu.g/mL.

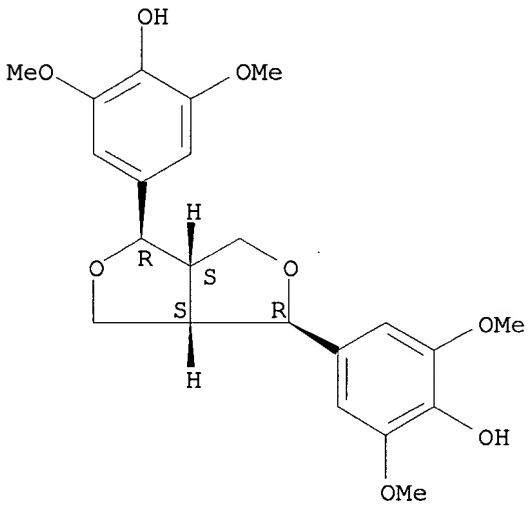
IT **6216-81-5**, Lirioresinol B **81446-29-9**, (-)-Pinoresinol

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(cytotoxic and anti-HIV principles from Leitneria floridana)

RN 6216-81-5 CAPLUS

CN Phenol, 4,4'-[(1R,3aS,4R,6aS)-tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl]bis[2,6-dimethoxy- (9CI) (CA INDEX NAME)

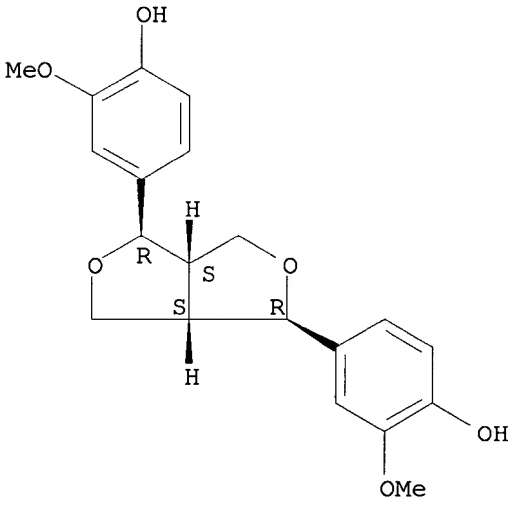
Absolute stereochemistry.



RN 81446-29-9 CAPLUS

CN Phenol, 4,4'-[(1R,3aS,4R,6aS)-tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl]bis[2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS

09591464

ACCESSION NUMBER: 1996:369715 CAPLUS
DOCUMENT NUMBER: 125:41748
TITLE: Extraction of anticancer and antiviral substances from Stellera chamaejasme for therapeutic use
INVENTOR(S): Ikegawa, Tetsuo; Ikegawa, Akiko
PATENT ASSIGNEE(S): Seimei Kagaku Kenkyusho Jugen, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

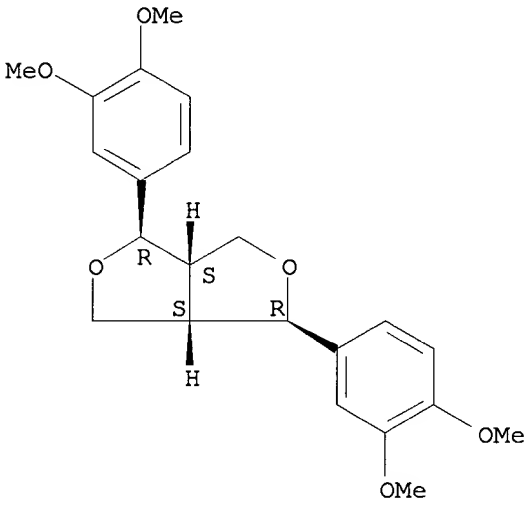
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08092118	A2	19960409	JP 1994-256052	19940927

AB Extn. of anticancer and antiviral gnidimacrin, stelleramacrin, eudesmin, and C15H22O3 (a novel compd.) from S. chamaejasme for therapeutic use is claimed. In antiviral activity tests, the compds. alone or in combinations were active against viruses esp. **AIDS** virus.

IT **526-06-7P**, Eudesmin
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(extn. of anticancer and antiviral substances from Stellera chamaejasme for therapeutic use)

RN 526-06-7 CAPLUS
CN 1H,3H-Furo[3,4-c]furan, 1,4-bis(3,4-dimethoxyphenyl)tetrahydro-, (1R,3aS,4R,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:224321 CAPLUS
DOCUMENT NUMBER: 114:224321
TITLE: Evaluation of natural products as inhibitors of human immunodeficiency virus type 1 (HIV-1) reverse transcriptase
AUTHOR(S): Tan, Ghee T.; Pezzuoto, John M.; Kinghorn, A. Douglas; Hughes, Stephen H.

09591464

CORPORATE SOURCE: Coll. Pharm., Univ. Illinois, Chicago, IL, 60612, USA
SOURCE: J. Nat. Prod. (1991), 54(1), 143-54
CODEN: JNPRDF; ISSN: 0163-3864
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inhibition of human immunodeficiency virus reverse transcriptase is currently considered a useful approach in the prophylaxis and intervention of acquired immunodeficiency syndrome (**AIDS**), and natural products have not been extensively explored as inhibitors of this enzyme. The reverse transcriptase assay developed for the detection of the enzyme in virions, involving poly rA.oligo dT and radio and radiolabeled thymidine 5'-triphosphate (TTP), can be applied as a simple method for screening the human immunodeficiency virus type 1 reverse transcriptase (HIV-1 RT) inhibitory potential of natural products; 156 pure natural products have been examd. in this system. Benzophenanthridine alkaloids such as fagaronine chloride (I) and nitidine chloride, which are known inhibitors of avian myeloblastosis virus reverse transcriptase, demonstrated potent activity in the HIV-1 RT system, and T(IC50 10 .mu.g/mL) was adopted as a pos.-control substance. Addnl. inhibitors found were columbamine iodide and other protoberberine alkaloids, the isoquinoline alkaloid O-methylpsychotrine sulfate, and the iridoid fulvoplumierin. A no. of indolizidine, pyrrolizidine, quinolizidine, indole, and other alkaloids, as well as compds. of many other structural classes, were found to be inactive. A total of 100 plant exts. have also been evaluated, and 15 of these exts. showed significant inhibitory activity. Because tannins and other polyphenolic compds. are potent reverse transcriptase inhibitors, methods were evaluated for the removal of these from plant exts. prior to testing. Polyphenolic compds. were found to be responsible for the activity demonstrated by the majority of plant exts. After appropriate tannin removal procedures were established, the bioassay system was shown to be generally applicable to both pure natural products and plant exts. The method also proved useful in directing an isolation procedure with Plumeria rubra to yield fulvoplumierin as an active compd. (IC50 45 .mu.g/mL).

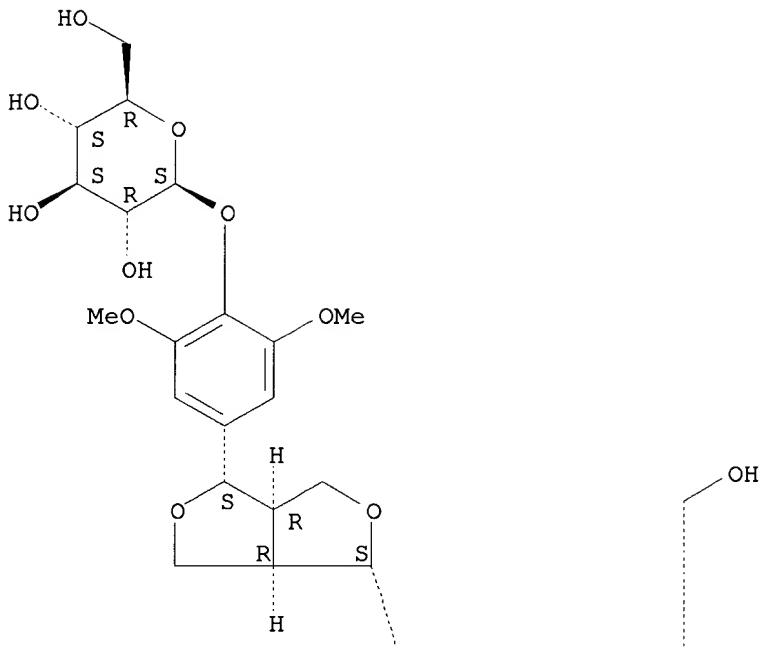
IT **573-44-4**, Liriodendrin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reverse transcriptase of human immunodeficiency virus type 1 inhibition by)

RN 573-44-4 CAPLUS

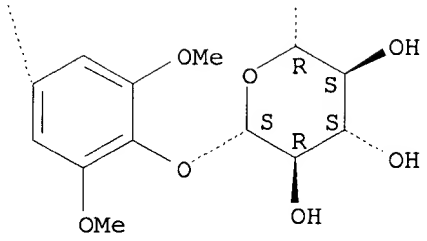
CN .beta.-D-Glucopyranoside, [(1S,3aR,4S,6aR)-tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl]bis(2,6-dimethoxy-4,1-phenylene) bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



L4 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:114648 CAPLUS
DOCUMENT NUMBER: 114:114648
TITLE: Differential in vitro anti-HIV activity of natural lignans
AUTHOR(S): Schroeder, Heinz C.; Merz, Helmut; Steffen, Renate; Mueller, Werner E. G.; Sarin, Prem S.; Trumm, Susanne; Schulz, Jutta; Eich, Eckart
CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Mainz, Mainz, D-6500, Fed. Rep. Ger.
SOURCE: Z. Naturforsch., C: Biosci. (1990), 45(11-12), 1215-21
CODEN: ZNCBDA; ISSN: 0341-0382
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two naturally occurring lignanolides, isolated from the tropical climbing shrub Ipomoea cairica,(-)-arctigenin and (-)-trachelogenin, inhibited strongly the replication of human immunodeficiency virus type 1 (HIV-1; strain HTLV-III B) in vitro. At 0.5 .mu.M, (-)-arctigenin and

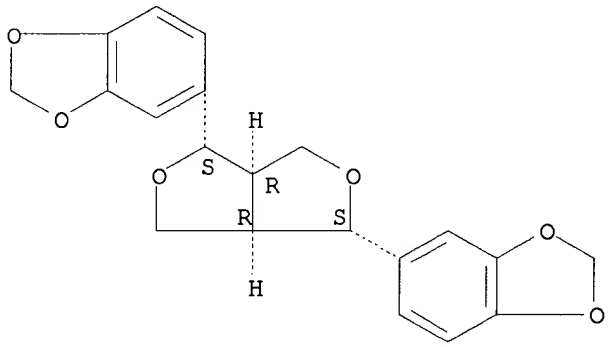
(-)-trachelogenin inhibited the expression of HIV-1 proteins p17 and p24 by 80-90% and 60-70%, resp. The reverse transcriptase activity in the culture media was reduced by 80-90% when the cells (HTLV-III B/H9) were cultivated in the presence of 0.5 .mu.M (-)-arctigenin or 1 .mu.M (-)-trachelogenin. At the same concns., the formation of syncytia in the HTLV-III B/H9-Jurkat cell system was inhibited >80%. A series of other lignan type compds. displayed no anti-HIV activity. Studying the mol. mechanism of action of (-)-arctigenin and (-)-trachelogenin, it was found that both compds. are efficient inhibitors of the nuclear matrix-assocd. DNA topoisomerase II activity, particularly of the enzyme from HIV-1-infected cells. Both compds. may prevent the increase of topoisomerase II activity, involved in virus replication, after infection of cells with HIV-1.

IT **607-80-7**, (+)-Sesamin **13060-15-6**, (+)-Aschantin
RL: BIOL (Biological study)
(HIV-1-inhibiting activity of, topoisomerase II in relation to)

RN 607-80-7 CAPLUS

CN 1,3-Benzodioxole, 5,5'-(tetrahydro-1H,3H-furo[3,4-c]furan-1,4-diyl)bis-, (1S,3aR,4S,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13060-15-6 CAPLUS

CN 1,3-Benzodioxole, 5-[tetrahydro-4-(3,4,5-trimethoxyphenyl)-1H,3H-furo[3,4-c]furan-1-yl]-, (1S,3aR,4S,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.